## REMARKS

Claim 5 is amended to remove recitation of the term "about." No new matter is added by the amendment. Claims 1-12 are presently under examination.

**Rejection under 35 U.S.C. § 112, first paragraph – Enablement**

Claims 1-12 are rejected under 35 U.S.C. § 112, first paragraph because the specification allegedly does not support the full scope of the claims. Specifically, the Office Action states that while the specification enables performing the claimed methods using HCl concentrations ranging from 0.1 N to 0.4 N, the specification does not enable the full scope of all concentrations of HCl because HCl at too high concentration would cause too much tissue damage and HCl at too low concentration would not induce a pathological effect. The Office Action concludes that since not all HCl concentrations will produce the desired nonbacterial prostatitis model phenotype, the specification does not enable the full scope of the claims.

Applicants respectfully traverse this rejection.

As detailed below, Applicants have provided specific teachings and Examples of how to prepare nonbacterial prostatitis animal models under several different HCl concentrations. One skilled in the art could simply follow the teachings and Examples of the specification to administer different HCl concentrations, and follow the teachings and Examples of the specification to evaluate the resultant effects in order to determine whether or not a particular HCl concentration yielded a suitable nonbacterial prostatitis animal model. The fact that one skilled in the art would have to perform one or more experiments in order to evaluate different HCl concentrations is insufficient to establish a lack of enablement. The fact that not all HCl concentrations may be suitable for establishing a suitable nonbacterial prostatitis animal model is insufficient to establish a lack of enablement. The facts must establish that the experimentation required to practice the full scope of the claims would be undue. No facts supporting such a conclusion are presently of record. Accordingly, the record does not support a holding that it would require undue experimentation to practice the full scope of the claims.

**Applicable Law**

A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 §U.S.C. 112, first paragraph, unless there is a reason to doubt

the objective truth of the statements contained therein which must be relied on for enabling support. As stated by the court, "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). M.P.E.P. §2164.04.

The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm"n 1983), *aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). See also *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). M.P.E.P. §2164.01. Thus, it is insufficient to provide evidence or reasoning establishing that further experimentation is necessary; the evidence or reasoning must establish that the further experimentation required would be undue.

The presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984) (prophetic examples do not make the disclosure nonenabling). M.P.E.P. §2164.08(b). Thus, it is insufficient to provide evidence or reasoning establishing that the claims encompass inoperative embodiments; the evidence or reasoning must establish that it would require undue effort to determine which embodiments were operative and which were inoperative.

For a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be used in that manner without undue experimentation. M.P.E.P. §2164.02. Thus, where numerous working examples are provided, a rejection as to undue breadth of a claim should not typically

be issued, and must be based on evidence or reasoning clearly demonstrating the requirement of undue experimentation to make or use the full scope of the claim.

**Teachings of the Specification and Working Examples**

The specification provides specific guidance and working Examples describing how to prepare candidate nonbacterial prostatitis animal models by injecting HCl, and how to evaluate these candidate nonbacterial prostatitis animal models to determine their suitability. For example, the specification at page 21, lines 26-30, and at Example 1 teaches, how to inject several different concentrations of HCl into an animal beneath the prostatic capsule in preparing a nonbacterial prostatitis animal model consistent with the claimed nonbacterial prostatitis animal models. Furthermore, the specification, at page 17, line 4, through page 18, line 22, and at Example 2, teaches particular pathohistological characteristics and methods for assessing these characterisitcs in evaluating the resultant injected animal to determine whether or not the animal would serve as a suitable nonbacterial prostatitis animal model. In addition, the specification, at page 18, line 23, through page 20, line 17, and at Example 3, teaches particular urine storage characteristics and methods for assessing these characteristics in evaluating the resultant injected animal to determine whether or not the animal would serve as a suitable nonbacterial prostatitis animal model.

**Knowledge and Skill in the Art**

The skill in the applicable art is high, typically including those with a Ph.D. in the relevant art and several years of laboratory experience. Those of skill in the art could readily follow the teachings of the specification and the Examples as described above with no more than routine experimentation to perform the disclosed methods and to assess the results.

There was thorough knowledge in the art with respect to human prostatitis, such as pathohistological characteristics of human chronic nonbacterial prostatitis, histological image shows, chronic inflammatory response and stromal strand hyperplasia and the infiltration of lymphocytes, plasma cells and macrophages at the periphery of a lobule is observed, often accompanying ductal basal cell hyperplasia, as exemplified by the reference cited in the specification: Surgical Pathology, Bunkodo, 1999, 793-794. Thus, one skilled in the art would readily be able to compare observed characteristics of an animal model generated with any of a variety of HCl concentrations with known human prostatitis conditions in order to evaluate the suitability of the animal model to a particular human prostatitis condition.

**Experimentation Required**

In order to determine whether or not any particular HCl concentration would be useful for establishing a nonbacterial prostatitis animal model, one skilled in the art could follow the teachings in the specification of injecting an animal with HCl beneath the prostatic capsule, and one skilled in the art also could follow the teachings of the specification as to pathohistological and urinary storage characteristics of the animal in assessing the affects of the HCl injection. One skilled in the art could then compare these characteristics to known characteristics of human prostatitis in order to determine whether or not the injected animal demonstrates characteristics suitable for a nonbacterial prostatitis animal model. There is no fact of record, nor any reasoning put forward in the Office Action, that would suggest one skilled in the art could not perform the above steps by routine experimentation. An enablement rejection cannot be supported by a finding that no more than routine experimentation is required to practice the full scope of the claim. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). M.P.E.P. §2164.01.

The Office Action states that HCl at too high concentration would cause too much tissue damage and HCl at too low concentration would not induce a pathological effect. While it may be true that not all HCl concentrations would be found suitable for establishing a suitable nonbacterial prostatitis animal model, such a fact is insufficient to establish a lack of enablement. There must be evidence or reasoning establishing that it would require undue effort to determine which embodiments were operative and which were inoperative. *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984). M.P.E.P. §2164.08(b). No such evidence is of record in this case. To the contrary, the teachings in the specification, the working Examples, and the knowledge in the art demonstrate that one skilled in the art with only routine experimentation could determine HCl concentrations for establishing suitable nonbacterial prostatitis animal models.

In conclusion, Applicants have provided specific teachings and Examples of how to prepare nonbacterial prostatitis animal models under several different HCl concentrations. One skilled in the art could by routine experimentation follow the teachings and Examples of the specification to administer different HCl concentrations, and follow the teachings and Examples of the specification to evaluate the resultant effects in order to determine whether or not a particular HCl concentration yielded a suitable nonbacterial prostatitis animal model. The fact that one skilled in the art would have to perform one or more experiments in order to evaluate

different HCl concentrations is insufficient to establish a lack of enablement. The fact that not all HCl concentrations may be suitable for establishing a suitable nonbacterial prostatitis animal model is insufficient to establish a lack of enablement. The facts must establish that the experimentation required to practice the full scope of the claims would be undue. No facts supporting such a conclusion are presently of record. Accordingly, the record does not support a holding that it would require undue experimentation to practice the full scope of the claims.

**Rejection under 35 U.S.C. § 112, second paragraph**

Claim 5 is rejected under 35 U.S.C. § 112, second paragraph as being indefinite. Specifically, the Office Action states that the term "about" in Claim 5 is indefinite.

Claim 5 is amended herein to remove the term "about." Accordingly, Applicants respectfully request removal of this ground for rejection of Claim 5.

**Rejection under 35 U.S.C. § 103**

Claims 1-12 are rejected under 35 U.S.C. § 103 Claims 1-12 as obvious over Lang, Keetch, Fulmer, Robinette, and Royston in view of Goto. Specifically, the Office Action states that it would have been obvious to combine the teachings of Lang of administering an irritant to prostate to develop a model of prostatitis with the teachings of Keetch, Fulmer and Robinette of administering other compositions to develop a model of prostatitis, with the teachings of Royston which teaches that HCl acts as a non-specific irritant and the teachings of Goto which teaches administration of HCl in developing a model of prostatitis.

Applicants respectfully traverse this rejection.

Applicants submit that the claimed nonbacterial prostatitis animal model is not obvious over the claimed references because no combination of these teaching would lead one to the presently claimed nonbacterial prostatitis model. In fact, the teachings of several references, if anything, would lead away from the claimed nonbacterial prostatitis model.

**Lang**

The Office Action states that Lang teaches use of an irritant in developing an animal model of prostatitis.

Lang teaches use of ethanol and DNBS to develop an animal model of prostatitis. Lang teaches that 3 of 5 animals died before the seventh post treatment day. *Lang* at page 203, left column, top paragraph. Thus, the skilled person would not seek to use the method of Lang in

developing a prostatitis model because such a model would result in more than half of the model animals dying of urethral obstruction by the seventh day of preparation. Accordingly, the high fatality rate of Lang serves as an example of reagents to avoid when developing an efficient animal model for prostatitis. As such, if anything, Lang teaches away from the claimed animal model.

**Fulmer, Robinette and Keetch**

The Office Action states that Fulmer, Robinette and Keetch support the teachings of Lang by using "other irritants or inflammatory agents" to induce prostatitis. *Office Action* at page 9.

Fulmer, Robinette and Keetch teach injection of various specific inflammatory substances to develop an animal model of nonbacterial prostatitis. However, these references do not teach or suggest use of HCl or any similar compound, such as an irritant, for inducing prostatitis. Accordingly, these references bear little relevance to the claims. Moreover, in view of the teachings of these references of the requirement of such specific inflammatory response-inducing substances for developing a prostatitis model, these references serves as evidence that administration of HCl would not be successful in developing a nonbacterial prostatitis animal model. Accordingly, these references demonstrate the non-obviousness of the claimed nonbacterial prostatitis animal model.

Fulmer teaches injection of lipopolysaccharide (LPS) beneath the capsule of a ventral prostate lobe. Fulmer teaches how LPS, a bacterial cell wall component, serves as the cause of Gram negative bacterial inflammation. *Fulmer* at page 248, left column, second paragraph and Figure 1. Thus, Fulmer teaches the use of LPS as a model of bacterial prostatitis. In contrast, the presently claimed methods are directed to nonbacterial prostatitis animal models exhibiting a prostate tissue damage characteristically observed in human chronic nonbacterial prostatitis and a lower urinary tract disorder characteristically observed in human chronic nonbacterial prostatitis. Nothing in Fulmer would lead one to suspect that a nonbacterial prostatitis animal model could be developed using LPS. Furthermore, because Fulmer teaches the unique bacterial inflammation response particular to LPS (Figure 1), nothing in Fulmer would lead one to use a compound such as HCl as a replacement for LPS in developing a prostatitis model, much less in developing a nonbacterial prostatitis model.

Further regarding Fulmer, as Applicants have explained in their specification at page 7, lines 19-22, and page 8, lines 6-7, that the prostatic tissue damage in the experiment by Fulmer is limited to the LPS injection site and the periphery thereof. *See, e.g., Fulmer* at page 249, right column, bottom paragraph ("The inflammatory infiltrate was primarily confined to the interstitial space with

few inflammatory cells present in the ductal lumen"). Accordingly, the administration of LPS as taught by Fulmer has a distinct disadvantage for the development of a prostatitis model.

Robinette teaches establishment of a model system for the hormonal induction of an inflammatory reaction in the rat lateral prostate. *Robinette* at Abstract. Robinette teaches castration and administration of estradiol-17β and subsequent insertion of a dihydrotestosterone implant to establish this model. Robinette teaches specific roles that these hormones play in prostate inflammation and prostate leukocyte infiltration. *Robinette* at 272, first two paragraphs. Moreover, Robinette teaches the importance of each of castration and time-sensitive sequential administration of the two hormones. *Robinette* at 284, third paragraph. Furthermore, as Applicants have described in their specification at page 7, lines 26-29, and at page 8, lines 7-15, Robinette's elaborate procedure takes a relatively long period of time (at least 3 to 4 weeks) to prepare the animal model by creating a hormonal imbalance by administration of hormones; and it is difficult to confirm that the hormones are securely administered during animal model preparation. For example, animal model preparation in accordance with the teachings of Robinette may fail due to hormone implant administration problems. Further, during preparation of the animal model, two operations are needed for castration and hormone implant insertion, thereby complicating the procedure. Thus, Robinette teaches unique inflammation response particular to estradiol-17β and dihydrotestosterone, and the requirement of an elaborate procedure for model development that includes castration and multiple time-sensitive administrations of these hormones. As such, no teaching in Robinette would lead one of ordinary skill in the art to suspect that such an elaborate method of developing a hormone-based prostatitis model could be substituted by a simple administration of a non-hormonal compound such as HCl in developing a nonbacterial prostatitis model. If anything, the requirement of the elaborate procedure taught by Robinette would lead one of skill in the art to doubt that administration of HCl could successfully establish a nonbacterial prostatitis model. Accordingly, Robinette's elaborate teachings serve as evidence of the non-obviousness of the presently claimed nonbacterial prostatitis model.

Keetch teaches injection of prostate homogenates from a variety of different mouse strains resulted in some mice developing prostatitis. Based on these findings, Keetch concluded that one or more specific prostate antigens induce prostatic inflammation via autoimmune response to yield an autoimmunity-based prostatitis model. *Keetch* at Abstract and at page 249, right column, last two paragraphs. Importantly, Keetch teaches that some of the injected prostate homogenates failed to cause any development of prostatitis, while other injected prostate homogenates caused inconsistent,

varying degrees of prostatitis, and only prostate homogenates from a specific strain, C57bl/6, caused consistent prostatitis. Thus, Keetch teaches that only a select subset of prostate homogenates can be used to generate an autoimmunity-based model of prostatitis, and that numerous other prostate homogenates would not be useful for reliably generating a prostatitis model. As such, Keetch teaches the unpredictability of even highly related substances in developing a reliable prostatitis model. Keetch provides evidence that one skilled in the art would not even be motivated to use a random prostatitis homogenate, much less HCl, for developing a reliable prostatitis model. Accordingly, Keetch serves as strong evidence in support of the non-obviousness of the present nonbacterial prostatitis animal model.

In conclusion, Fulmer, Robinette and Keetch all teach use of specific inflammation-inducing substances in generating prostatitis models. Nothing in any of these references suggests than anything other than very specific administrations and/or administration methods can be successful in generating a prostatitis model. Robinette and Keetch teach that not even minor variations of their methods can be made without destroying the reliability of the prostatitis model. As a result, these references serve as evidence of the non-obviousness of Applicants claims and provide no basis whatsoever for the injection of HCl in developing a nonbacterial prostatitis animal model.

**Roysten**

The Office Action states that Royston teaches that HCl is a non-specific irritant that initiates inflammation in tissues.

Royston teaches HCl-induced injury to rat lung. Royston concludes that HCl will initiate a severe inflammatory response in rat lung. Royston teaches or suggests nothing about the effect of administration of HCl to prostate. In fact, Royston teaches or suggests nothing about the effect of administration of HCl to any tissue other than lung. No basis is provided in Royston or any other reference of record to conclude that HCl will have the same affect in any tissue to which it is administered. Furthermore, no basis is provided in Royston to conclude that HCl could be used to initiate an inflammatory response in prostate of the character and nature that would result in prostate tissue damage characteristically observed in human chronic nonbacterial prostatitis and a lower urinary tract disorder characteristically observed in human chronic nonbacterial prostatitis. Furthremore, nothing in Royston teaches or suggests that injecting HCl beneath the prostatic capsule would cause this an inflammatory response in prostate of the character and nature that would result in prostate tissue damage characteristically observed in human chronic nonbacterial prostatitis and a lower urinary tract disorder characteristically observed in human chronic

nonbacterial prostatitis. At most, it may have been obvious to try the general approach Royston as a promising field of experimentation, where Royston gave no more than general guidance as to the particular manner for generating an inflammatory response in an animal. However, it is well established as impermissible to base an obviousness rejection on such reasoning. *See, e.g., In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988); and *M.P.E.P.* §2145 X.B. Accordingly, the teachings of Royston cannot support the obviousness rejection of the claims.

**Goto**

The Office Action states that Goto teaches the use of HCl in the production of a prostatitis model.

Goto teaches developing animal models of bacterial prostatitis by pretreatment of the vas deferens of animals with HCl prior to administration of *E. coli*. Further, Goto also teaches developing animal models of bacterial prostatitis without HCl pretreatment. Accordingly, Goto teaches that HCl is optional and that bacteria are essential for development of Goto's animal models. In contrast, the presently claimed methods are directed to nonbacterial prostatitis animal models exhibiting a prostate tissue damage characteristically observed in human chronic nonbacterial prostatitis and a lower urinary tract disorder characteristically observed in human chronic nonbacterial prostatitis. Nothing in Goto would lead one to suspect that a prostatitis animal model could be developed without the use of bacteria. Thus, nothing in Goto would lead one in any particular direction toward developing a nonbacterial prostatitis model.

Furthermore, Goto's treatment of the vas deferens of animals with HCl is insufficient to develop a suitable prostatitis model. The examples of Applicants' specification show that treatment of the vas deferens with HCl results in only slight development of prostatits. In particular, the specification, at page 39, lines 1-33 and Figures 1 and 2, teaches that treatment of the vas deferens with HCl results in temporary damage that is no longer present after 4 days, rendering this mode of administration unsuitable for developing a prostatitis model. Therefore, one skilled in the art, when performing Goto's HCl administration in the absence of bacteria, would realize that such administration would be unsuccessful in establishing a prostatitis model. Further, one skilled in the art, when performing Goto's HCl administration in the presence of bacteria, would realize that such administration would be suitable for establishing a bacterial prostatitis model, but not a nonbacterial prostatitis model. Accordingly, Applicants' specification demonstrates that the teachings of Goto could not lead one of ordinary skill in the art to develop a nonbacterial prostatitis model.

**Conclusion**

Of the six references cited as evidence of the obviousness of Claims 1-12, one (Lang) teaches the high failure rate of their prostatitis model, and two (Robinette and Keetch) teach the importance of very specific hormonal and antigenic reagents, respectively, in order to establish prostatitis models; the teachings of these three references, if anything, would lead away from the use of HCl in preparing a nonbacterial prostatitis animal model. Of the remaining three references, two (Fulmer and Goto) are directed to development of bacterial prostatitis models, not nonbacterial prostatitis models, and one (Roysten) is not relevant to any aspect of study of the prostate.

No combination of these references would lead one of ordinary skill in the art to develop a nonbacterial prostatitis animal model exhibiting a prostate tissue damage characteristically observed in human chronic nonbacterial prostatitis and a lower urinary tract disorder characteristically observed in human chronic nonbacterial prostatitis, where the animal model is a nonhuman animal, and is prepared by injecting hydrochloric acid beneath the prostatic capsule. Furthermore, numerous teachings in these references support the non-obviousness of the claimed nonbacterial prostatitis animal model. Accordingly, the nonbacterial prostatitis animal model of Claim 1, and the subject matter of all claims dependent from Claim 1, are not obvious over the cited references.

**CONCLUSION**

In view of the above, Applicants respectfully maintain that claims are patentable and request that they be passed to issue. Applicants invite the Examiner to call the undersigned if any remaining issues might be resolved by telephone.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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